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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,864	10/15/2001	Henryk Dudek	CIBT-P01-104	3719

28120 7590 03/17/2008

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PATENT DOCKETING 39/41
ONE INTERNATIONAL PLACE
BOSTON, MA 02110-2624

EXAMINER	
HOWARD, ZACHARY C	

ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
03/17/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/977,864	DUDEK ET AL.	
	Examiner	Art Unit	
	ZACHARY C. HOWARD	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-9,21 and 23-60* is/are pending in the application.

4a) Of the above claim(s) *4 and 6-9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,21 and 23-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,4-9,21 and 23-60* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 April 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :11/23/07;12/13/07;1/25/08;2/1/08.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 12/13/07 has been entered in full. Claims 3, 10-13, 19 and 20 are canceled. Claims 1, 5, 21, 23 and 24 are amended. New claims 26-60 are added.

Claims 4 and 6-9 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. It is noted that withdrawn claim 4 depends from canceled claim 3. It is noted that withdrawn claims 6, 7 and 8 each depend from claim 5 but recite species of cancer that are not encompassed by amended claim 5. It is noted that withdrawn claim 9 depends from claim 1 but recites a species of unwanted cell proliferation that is not encompassed by amended claim 1.

Claims 1, 5, 21 and 23-60 are under consideration in the instant application, as they read upon the elected species of colon cancer and hedgehog antibody.

Information Disclosure Statement

The Information Disclosure Statements filed on 11/23/07; 12/13/07; 1/25/07 and 2/1/08 have each been considered.

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (9/11/07).

All rejections of claim 3 are moot in view of Applicants' cancellation of this claim.

The objection to claim 1 at pg 11 is *withdrawn* in view of Applicants' amendments to the claims that replace "overexpress" with "overexpresses".

The rejection of claims 1, 5, 21 and 23-25 under 35 U.S.C. § 112, first paragraph at pg 3-9 for failing to comply with the written description requirement is *withdrawn* in view of Applicants' amendments to the claims and Applicants' persuasive arguments at pg 10-15 of the 12/13/07 response.

The provisional rejection of claims 1, 5, 21 and 23-25 at pg 9-11 under the judicially created doctrine of obviousness-type double patenting as being unpatentable

over claim 25 of copending Application No. 10/652,298 is *withdrawn* in view of the 12/26/07 amendments to the claims in the '298 application which limit the measured gene in the method of claim 25 to a "*Sonic hedgehog* gene". The instant claims are limited to methods comprising measurement of a "*gli-1* gene".

The rejection of claim 21 under 35 U.S.C § 112, second paragraph, at pg 11-12 for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is *withdrawn* in view of Applicants' amendments to the claim.

The rejection of claim 1 under 35 U.S.C. § 102(b) at pg 12-13 as being anticipated by Wallace et al (1999) is *withdrawn* in view of Applicants' amendments to the claim.

The rejection of claim 1 under 35 U.S.C. § 103(a) at pg 13-14 as being unpatentable over Dahmane et al #1 (1997) in view of Dahmane et al #2 (1999) is *withdrawn* in view of Applicants' amendments to the claim.

New rejections necessitated by Applicants' amendment

Claim Rejections - 35 USC § 112, 1st paragraph, enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 60 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method for treating colon cancer, comprising determining whether colon cancer tissue overexpresses a *gli-1* gene and administering to a patient in need thereof an amount of a *hedgehog* antibody sufficient to decrease at least one of the growth or proliferation of the colon cancer tissue, wherein the colon cancer tissue overexpresses a *gli-1* gene, and wherein the *hedgehog* antibody binds to Sonic hedgehog protein and inhibits *hedgehog* signaling,

does not reasonably provide enablement for:

a method for treating colon cancer, comprising administering to a patient in need thereof an amount of a *hedgehog* antibody sufficient to decrease at least one of the growth or proliferation of the colon cancer tissue, wherein the *hedgehog* antibody binds to Sonic hedgehog protein and inhibits *hedgehog* signaling.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention of claim 60 is a method of treatment of colon cancer comprising administration of an anti-Sonic hedgehog antibody. Claim 60 differs significantly from the other pending claims in that (1) it does not require measurement of *gli-1* gene expression and (2) it does not require that the treated cancer tissue is cancer tissue that overexpresses *gli-1*.

However, the specification provides limited teachings regarding whether or not the claimed methods will work to treat colon cancer (the elected species under consideration) that does not overexpress the *gli-1* or *Sonic hedgehog* (*Shh)* gene. The specification teaches (pg 136-139) that high levels of *gli-1* expression (as compared with "non-proliferative" cells) can be found in some tumors of the prostate, lung, and breast (e.g., "6 out of 15 prostate cancer samples all showed strong gli1 expression"; pg 136). The specification further teaches that the *gli-1* and *Shh* genes are overexpressed in some bladder tumors as compared with normal bladder (pg 144). The specification further teaches that the anti-Shh antibody 5E1 inhibits tumor growth in nude mice injected with the bladder or colon cell lines (pg 146-147; pg 152-153). With respect to the colon cancer cell lines, the specification teaches that an anti-hedgehog antibody

(5E1) "significantly decreases tumor size, weight, and rate of growth in comparison to that of mice treated with PBS (Figures 36 and 37; see pg 152-153).

Significantly, in U.S. Pre-Grant Application Publication 2004/0110663 (a publication of application 10/652,298, which is a continuation-in-part of the instant application), Applicants report that the growth of a xenograft of non-hedgehog expressing colon cancer cell line SW480 is not inhibited by 5E1 (Figure 54; ¶ 848 of the '663 publication). Furthermore, the relevant art teaches that "[c]ell lines might not be good models for the assessment of Hh pathway activity. However, the published results on primary human colon cancers are also confusing. Some authors, but not others detected increased levels of Hh pathway members during colon cancer progression. Moreover, the expression of Ihh and Gli1 were shown to be decreased during colon cancer progression in recent publications" (see pg 2626 of Chatel et al, 2007. Int J Cancer. 121: 2622-2627). In view of these teachings, the specification does not teach the skilled artisan how to treat colon cancer tissue that does not overexpress the *gli-1* or *Shh* genes as compared to normal tissue.

Due to the large quantity of experimentation necessary to determine whether or not an anti-Sonic hedgehog antibody could be used to treat colon cancer that does not overexpress the *gli-1* or *Shh* genes; the lack of direction/guidance presented in the specification regarding the same; the absence of working examples directed to the same; the complex nature of the invention; and the unpredictability of the effects of an anti-Sonic hedgehog antibody on colon cancer that does not overexpress the *gli-1* or *Shh* genes, undue experimentation would still be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 5, 21 and 23-60 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 5 of copending Application No. 10/652,298. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

It is noted that the claims of '298 application were amended on 12/26/07. The amendments to the instant claims and the claims of '298 application necessitate this new provisional rejection.

Each of instant claims 1, 5, 23, 24, 26 and 33 fully encompasses the method of claim 5 of the '298 application. Claim 5 of the '298 application depends from claim 1, and encompasses a method comprising determining whether diseased tissue overexpresses a *gli-1* gene, and contacting an overexpressing tissue with an anti-Sonic hedgehog antibody that inhibits *hedgehog* signaling in order to treat the cancer, wherein the tissue is associated with urogenital cancer and colon cancer. While the instant claims do not recite that the cancer is associated with both urogenital cancer and colon cancer, they do recite that the cancer is associated with one or more of a group including colon cancer. Due to the use of open-type language in the instant claims (i.e., "a method ... comprising …", these claims encompass methods performed with cancer associated with colon cancer and urogenital cancer. Therefore, claim 5 of the '298 anticipates each of instant claims 1, 5, 23, 24, 26 and 33.

Claims 21, 25, 27-32 and 60 are of similar scope to instant claim 1, but limit the method to one performed in a patient (i.e., *in vivo*). The specification of the '298 application indicates that *in vivo* treatment is a preferred embodiment of the claimed methods; therefore, claim 5 also anticipates instant claims 21, 25, 27-32 and 60.

New claims 34-39 depend from one of the above claims and limit the parent claim to one wherein the gene measurement is made in a sample obtained from a tumor in a patient. This further limitation is also a preferred embodiment of the '298 application, as evidenced by new claim 72 (presented 12/26/07 in the '298 application). Therefore, claim 5 of the '298 application also anticipates new claims 34-39.

New claims 40-59 each depend from one of the above claims and limit the parent claim to one wherein the *gli-1* overexpression is determined by measuring protein or transcript. These further limitations are also preferred embodiments of the '298 application, as evidenced by new claims 76 and 77 (presented 12/26/07). Therefore, claim 5 of the '298 application also anticipates new claims 40-59.

In the 12/13/07 response (pg 15), Applicants "contend that the claims, as amended, in the instant and co-pending applications are patentable in view of each other. Nevertheless, Applicants ask that this rejection be held in abeyance until indication of allowable subject matter. Applicants will submit a terminal disclaimer, if necessary, upon indication of allowable subject matter".

The Examiner notes Applicants' intention of submitting a terminal disclaimer; however, the rejection is maintained. See MPEP 804.I.B: "The "provisional" double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in at least one of the applications."

Conclusion

No claims are allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Z. C. H./
Examiner, Art Unit 1646

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646